

In the Claims:

In claim 10, line 4, after "than", insert --50--.

REMARKS

Claims 1-22 are pending in this application.

Applicant is pleased to note that claims 5-7 were allowed.

The specification has been amended to include a cross-reference to Applicant's International application.

Claim 10 has been amended to more particularly point out and distinctly claim the subject matter which Applicant regards as his invention, by including in the claim, the pore size of 50 Å, the numerical value having been inadvertently omitted from claim 10 as filed. This amendment is supported at page 9, line 22 of the application and therefore, no new matter has been added. The amendment is for purposes of clarification only, and is not being made to overcome the prior art in any way.

No new matter has been added to the application by any of the amendments.

At page 2, paragraph 1 of the Office Action, the Examiner stated that the Information Disclosure Statement filed June 10, 1997 (hereinafter "Applicant's IDS") does not comply with 37 C.F.R. § 1.98(a)(3) because it does not provide a concise explanation of the relevance of the cited German language reference DE 33 10 263 A1 (hereinafter the "German Reference"), since the German Reference is not in the English language. In addition, it is noted that on the Form PTO-1449 filed with Applicant's IDS, the Examiner has stricken out the German Reference listed on the form. It is respectfully submitted that the Examiner's determination that Applicant's IDS does not comply with 37 C.F.R. § 1.98(a)(3) and the striking of the German Reference from the Form PTO-1449 are improper. The German Reference was cited in the English language International Search Report from the PCT application, a copy of which was filed with the present application. According to MPEP Section 609 in the paragraph bridging pages 600-95 and 600-96, this is sufficient description of the German Reference, and the Examiner is therefore required to consider this foreign language reference. A copy of this portion of the MPEP, highlighted for the Examiner's convenience, is attached hereto.

Consideration and citation of the German Reference, and an acknowledgment of such consideration in the next Office Action are therefore respectfully requested.

The present invention is directed towards treatment in a discontinuous flow system of a blood plasma, serum and other suitable fraction (hereinafter referred to together as "plasma"). Plasma is a complicated mixture of ionic constituents, proteins, albumen, proteins and the like. Plasma is also characterized by parameters such as pH and enzyme activities. Any change in concentrations of the constituents, pH or denaturation of proteins is potentially fatal to a patient. Accordingly, extraction techniques which may be considered standard for treating chemical compositions may be quite unsuitable for treating blood and blood products. For example, Applicant has observed that solvents such as chloroform and hexane which are considered to be standard solvents for the removal of fatty acids from aqueous mixtures cause denaturation of proteins in plasma. Applicant therefore submits that techniques or procedures which are known to practical organic chemists, would not be considered to be known or obvious to those of ordinary skill in the art of treating blood products.

Claim Rejections - 35 U.S.C. § 102

Claims 1, 2 and 15 - 22 have been rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent 4,895,558 of Cham (hereinafter "*Cham*"). The comments made by the Examiner in relation to lipid apheresis and LDL apheresis are acknowledged. However, Applicant respectfully points out that the techniques of lipid apheresis and LDL apheresis are quite distinct. Lipids are present in blood plasma in association with apolipoproteins such as low density lipoproteins (LDL) and their associated apolipoproteins. In LDL apheresis, the proteins as well as the lipids are removed. On the other hand, lipid apheresis selectively removes the lipids, the apolipoproteins remain in the plasma and are ultimately returned to the patient. The advantages of lipid apheresis over LDL apheresis are discussed in the introductory portion of the present specification. One such advantage is the surprising discovery that with lipid apheresis, the apolipoproteins which are returned to the patient are able to mobilize deposited fats such as cholesterol in arteries, plaques and the like. These mobilized materials are then subject to

removal in a further apheresis step. This mobilization and subsequent removal is not possible with LDL apheresis.

With further reference to *Cham*, this document discloses a continuous lipid apheresis procedure. Claim 1 of the present application, the only independent claim, recites a discontinuous procedure in which the solvent extraction step is carried out separately and remotely from the subject. There is no disclosure in *Cham* as to a discontinuous system. Accordingly, Applicant submits that claims 1, 2 and 15 - 22 are not anticipated by *Cham*.

Applicant further submits that modifying *Cham* to a discontinuous procedure would not have been obvious. *Cham* teaches the advantages of a continuous system in that the patient's own blood is directly returned to the patient. Thus there is no problem with rejection or antibody production. It also avoids the needs for storage and transport of the blood or blood fraction. Applicant submits that there is no teaching, suggestion or incentive in *Cham* as to a discontinuous lipid apheresis procedure.

Claim Rejections 35 U.S.C. § 103

Claims 8 - 14 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over *Cham* in view of U.S. Patent 5,401,415 of *Rauh et al.* (hereinafter "*Rauh*").

Rauh describes LDL apheresis. As stated above, LDL apheresis is a completely distinct process from lipid apheresis. *Rauh* describes the use of an absorption material for the selective removal of LDL cholesterol. The absorption material is a solid phase ligand and preferable ligands are those with a 1,2-dihydroxypropyl-3-oxypropyl residue. These materials bind to LDL (see column 4, lines 33 to 43). The passages referred to by the Examiner at column 1, lines 47 - 64 also describe procedures by which LDL are specifically adsorbed. The present invention is directed towards the selective removal of the lipids from plasma, while returning the proteins to the patient. *Rauh* on the other hand is directed towards a system in which the apolipoproteins are selectively adsorbed. Accordingly, it is submitted that *Rauh* teaches away from the present invention.

In relation to the sintered spheres as employed in the present invention, these spheres are for the selective removal of residual solvent such as 1-butanol from the blood fraction. These spheres do not absorb LDL. Accordingly, Applicant submits that the beads of

Rauh cannot be considered to have the characteristics of the sintered spheres as claimed in claims 9 - 11, 13 and 14.

With regard to claim 12, the Examiner says that it would have been obvious to pass the delipidated fraction through the absorbent at least twice. The comments made above in relation to the absorbent are reiterated. As the use of the absorbents is not obvious in view of *Rauh*, it is submitted that the process described in claim 12 is also not obvious.

Claim 3 has been rejected under 35 U.S.C. § 103(a) as being unpatentable over *Cham* as it would have been obvious to multiply the effect of washing by washing four times. Applicant submits that it would not have been obvious to treat the blood fraction by washing with the solvent four times in view of *Cham*. The comments made above in relation to the differences between standard organic extraction procedures and treatment of blood fractions are reiterated. Treatment of a blood fraction with organic solvents is a potentially hazardous procedure in view of the many adverse effects the solvent may have on the blood fraction. While repeated washing may be known in the organic chemistry laboratory, it is submitted that such treatment would not be obvious to a person of ordinary skill in the art of treating blood fractions. The potentially hazardous effects of treating blood fractions with organic solvents would be known by a person skilled in the art of treating blood products. Applicant therefore submits that the general knowledge of the person skilled in the art relating to this invention would have taught away from repeated washing. Thus, in view of the potentially hazardous effects of introducing organic solvents to a blood fraction, it is submitted that what would have been obvious would be to minimize solvent contact with the blood fraction and not to repeatedly introduce an organic solvent into a blood fraction as claimed in claim 3.

In regards to claim 4, the Examiner says that it appears that the method would work equally well with various other solvents. Applicant again reiterates the comments made above in relation to treatment of blood products. Applicant submits that it is not a simple matter of selecting a solvent according to polar characteristics. The effect of the solvent on the blood fraction and potential toxicity to the patient must also be taken into account. Such effects are not taught by the cited references.

In view of the distinctions pointed out above between the present invention and *Cham* and *Rauh*, whether considered alone or taken together, Applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. § 102 and 103.

In the Office Action Summary page, under the heading "Priority under 35 U.S.C. § 119", it is not clear whether the Examiner indicated that none of the certified copies of the priority documents have been received, since there just may be a printing registration error in the printing of the form. In any event, to clarify the matter, enclosed are copies of Form PCT/IB/304 and Form PCT/IB/308, respectively mailed January 24, 1996 and June 27, 1996, concerning Applicant's corresponding International PCT Application No. PCT/AU95/00875. These notifications relate to acknowledging receipt by the International Bureau of the priority documents and the communication of the International application to various designated offices, including the U.S. Under PCT Rule 47.1(c), the notice "shall be accepted by all designated offices as conclusive evidence that the communication has duly taken place on the date specified in the notice." Here, that date is June 27, 1996. Accordingly, it is respectfully submitted that Applicant's foreign priority under the corresponding International application and the underlying Australian priority application PN 0307, filed December 22, 1994, has been perfected. Acknowledgment of this matter is respectfully requested.

Reconsideration and withdrawal of the rejections, consideration and acknowledgment of the German reference and the acknowledgment of the perfection of the claim of foreign priority are all respectfully solicited, as is an early Notice of Allowance.

A Notice of Change of Address for the undersigned attorney and others in his law firm, all being attorneys of record, is also enclosed.

Respectfully submitted,

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May 21, 1998

(Date)

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